Comparative transcriptomic analysis of SARS-CoV-2 infected cell model systems reveals differential innate immune responses.

Journal: Sci Rep

Publication Year: 2021

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PubMed link: 34433867

Funding Grants: Combating COVID-19 using human PSC-derived NK cells

Public Summary:
In this study, we show that SARS-CoV-2 can establish a robust infection in HEK293T cells that overexpress the major SARS-CoV-2 host receptor, human angiotensin-converting enzyme 2 (hACE2), without triggering significant host immune response. Instead, stress response-related pathways are predominantly activated. By comparing our data with published transcriptome of SARS-CoV-2 infection, we found that the expression level of hACE2 directly correlates with the SARS-CoV-2 viral load in infected cells but not with the scale of immune responses. Only cells that express high level of endogenous hACE2 exhibit an extensive immune attack even with a low viral load. Therefore, the infection route may be critical for the extent of the immune response, thus the severity of COVID-19 disease status.

Scientific Abstract:
The transcriptome of SARS-CoV-2-infected cells that reflects the interplay between host and virus has provided valuable insights into mechanisms underlying SARS-CoV-2 infection and COVID-19 disease progression. In this study, we show that SARS-CoV-2 can establish a robust infection in HEK293T cells that overexpress human angiotensin-converting enzyme 2 (hACE2) without triggering significant host immune response. Instead, endoplasmic reticulum stress and unfolded protein response-related pathways are predominantly activated. By comparing our data with published transcriptome of SARS-CoV-2 infection in other cell lines, we found that the expression level of hACE2 directly correlates with the viral load in infected cells but not with the scale of immune responses. Only cells that express high level of endogenous hACE2 exhibit an extensive immune attack even with a low viral load. Therefore, the infection route may be critical for the extent of the immune response, thus the severity of COVID-19 disease status.